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U. S. ARMY MEDICAL RESEARCH & NUTRITION LABORATORY

PHYSIOLOGICAL AND BIOCHEMICAL EVALUATION OF POTENTIAL ANTI-FATIGUE DRUGS I THE EFFECTS OF ASPARTIC ACID SALTS (MG AND K) ON THE PERFORMANCE OF MEN

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US ARMY MEDICAL RESEARCH AND NUTRITION LABORATORY
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Report on

PHYSIOLOGICAL AND BIOCHEMICAL EVALUATION OF POTENTIAL ANTI-FATIGUE DRUGS. I. THE EFFECTS OF ASPARTIC ACID SALTS (Mg and K) ON THE PERFORMANCE OF MEN

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OBJECT:

This study was designed to investigate the use of magnesium and potassium salts of aspartic acid (Spartase, one of the so-called anti-fatigue agents), as a possible means of increasing endurance and prolonging the onset of fatigue in humans.

SUMMARY:

The performance of 12 men was measured during a 9 week study. Six of the men received placebos and 6 received 2 gm of magnesium and potassium salts of aspartic acid (Spartase) daily during 5 weeks of therapy.

There was no significant difference in metabolic rate and RQ between the control or Spartase supplemented groups during moderate exercise and the recovery period after moderate exercise. Differences in other factors such as maximum breathing capacity, vital capacity, etc. were also non-significant. A significant difference was observed between the groups during the last week of therapy in breath holding time. This was also true for the neuromuscular excitability time values after the exhausting run, which were significantly different only during the 4th week of therapy and not during the 5th week. It is questionable whether these two differences could be attributed to Spartase therapy since these differences were also observed two weeks after the discontinuance of therapy.

Under the stresses imposed in this study there seemed to be no convincing evidence of the beneficial effects of Spartase therapy.

APPROVED:

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PHYSIOLOGICAL AND BIOCHEMICAL EVALUATION OF POTENTIAL ANTI-FATIGUE DRUGS. I. THE EFFECTS OF ASPARTIC ACID SALTS (Mg and K) ON THE PERFORMANCE OF MEN

Background

During the past few years several French investigators (1, 2, 3) have reported the beneficial effects of potassium and magnesium salts of aspartic acid (Spartase) as a means of reducing fatigue at the neuromuscular level. Laborit, et al. (1, 2) postulated that "aspartic acid which functions in an intermediate position in the Krebs cycle should provide a suitable substrate for the increase of metabolic efficiency or delay of metabolic exhaustion. The magnesium ions act as a catalyst for the retransfer of potassium ions across the cell wall, while the potassium ions aid in maintaining a proper ionic balance". The possible value of aspartic acid salts was tested using the rat swimming test (Laborit, et al.) (3) (Rosen, et al.) (4). It was reported that the onset of exhaustion, was significantly and consistently delayed by the administration of aspartic acid salts.

It has been postulated that the electronic Rheotome can be used to evaluate neuromuscular fatigue (5). The Rheotome is used to measure the nerve-muscle reactions to electrical stimulation of a square wave nature with varying intensities and durations. From this information, intensity-duration curves are drawn. A better functional state of the individual is supposedly indicated by a greater nerve-muscle differential and vice versa. Changes in this differential between nerve and muscle excitability have been reported after training (5).

Agersborg and Shaw '61 (6) have studied the effect of Spartase in more than 2,000 patients, and observed that 80% of the subjects felt that they had experienced subjective signs of relief from fatigue. They also noted a placebo response in 20 - 26% of the subjects. In another study on 163 subjects (Shaw, et al. '62) (7) it was also reported that there was some objective and subjective evidence of relief from fatigue. It was reported that the clinical responses correlated fairly well with the objective results obtained with the electronic Rheotome. The objective measurements showed that the spread between muscle and nerve curves was increased in 7 of the 9 patients, 5 of whom experienced subjective improvement.

Several other investigators, Kruse (8), Taylor (9) and Chesney and Tullis (10) have also reported clinical studies on the beneficial effects of these magnesium and potassium salts of aspartic acid. Most of these studies were of a subjective nature, on patients who were basically complaining of chronic fatigue. They reported that when placebos were substituted in one-half of the patients, the symptoms of tiredness usually returned.

Experimental Design

The test subjects were 12 healthy men ranging in age from 20 - 48 years. They were arrayed in order of body weight and paired off. Each pair was then randomly divided between treatment A and treatment B. By a toss of a coin treatment group A was assigned "placebo" and treatment group B was assigned Spartase, however, the subjects were not informed which group they were in or what medication they were receiving.

The study continued for 9 weeks including (a) a 2 week preliminary control period designed for training, (b) 5 weeks of therapy, either with Spartase or placebo, and (c) 2 final weeks of control or recovery. Medication was taken orally twice daily, 2 tablets at 8 a.m. and 2 at 4 p.m. during the therapy period. Each Spartase tablet contained 500 mg of potassium and magnesium salts of aspartic acid.

The order of exercise for the subjects within each group was determined randomly at the start of the experiment. Thereafter, each man exercised at the same time each day, 5 days a week for 30 minutes. The exercise consisted of a brisk walk on a motor driven treadmill at 4.0 mph on a 3.5% grade (3.5 inches of height/100 inches of horizontal travel).

Oxygen consumption, carbon dioxide production and respiratory quotients were measured on each man twice a week during the last 15 minutes of exercise and for 10 minutes following the cessation of exercise. These measurements were taken continuously with an infra-red carbon dioxide analyzer, a Pauling type oxygen analyzer, and a recording dry gas meter for expired gas volumes (11).

"Neuromuscular excitability curves" or "strength duration curves" were determined on each subject once a week with an electronic Rheotome (TECA Corp., White Plains, New York), both before and immediately after exercise. When a nerve or muscle is electrically stimulated, the resulting contraction is dependent on the character, intensity and duration of the stimulus (12). The nerve or muscle is stimulated with a rectangular wave electrical signal. The intensity of the stimulus must be increased to produce contractions as the duration of applied stimulus is decreased. The "strength duration curve" is formed when the intensity of the stimulus required for a stimulation is plotted against the duration of time the stimulus is applied. Under normal conditions, the nerve is more excitable than the muscle and as a result the curve lies lower than the muscle when plotted. The distance between the curves for nerve and muscle is supposedly an indication of the functional state of the individual, a greater distance representing a better functional condition (7).

Timed vital capacities for one and two seconds, and maximum breathing capacities were determined with a 13.5 liter water sealed respirometer. Each measurement was done in duplicate and the mean of the two determinations used. Duplicate measurements of maximal breath holding were made against a stop watch following a maximum inhalation. Grip strength of the right and left hand were each done in duplicate with a hand dynamometer.

Twice during the therapy period (one week before the end of, and on the last day of the therapy period), and on the last day of the recovery period each subject performed a maximum run on the treadmill at 7.0 mph and 8.0% grade. The running time was noted and pulse counted from 1 - 1.5, from 2 - 2.5, and from 4 - 4.5 minutes after the cessation of the run, from which the "physical fitness index" was determined (13). Neuromuscular excitability curves were determined on each man before and immediately after the exhausting performance.

Differences between groups and within groups were tested for statistical significance. The principle test was the t-test applied to mean differences or individual differences as appropriate. Evaluation was at the 5% probability level.

Results

The men were assigned to treatment groups in part by body weight which initially averaged 79.16 and 75.62 kg for the control and Spartase groups, respectively (Table I). The body weight changes during the study were negligible, averaging -0.41 and -0.21 kg at the end of the study, for the same groups. Even though age and height were not specifically considered in assigning men to the groups the averages were exactly the same for the two groups, 28 years for age and 175 cm for height.

The respiratory quotients (RQ) determined for each man were averaged for each week for the 15 minutes of exercise, as well as for the two 5 minute recovery periods (Table II). There was no significant difference between the two groups throughout the study during the 15 minutes of exercise and the first 5 minutes of recovery. During the second 5 minutes of recovery, the Spartase group had a significantly higher RQ ($P < 0.025$) than the control group in the 8th and 9th weeks (recovery periods) but the differences during the weeks of therapy were non-significant. The oxygen consumption and carbon dioxide production values for each man were also averaged for each week. The weekly means of the oxygen consumption and carbon dioxide production values during exercise, and the two recovery periods are presented in Tables III and IV. The differences between the control and Spartase means were not significant in any week.

The oxygen debt data accumulated during the walk are shown in Table V and in no instance were the control and Spartase groups significantly different.

The original plan was to convert the oxygen consumption, carbon dioxide production and oxygen debt values to a common level of ml/kg of body weight, but since the weight changes were negligible these computations were unnecessary.

Forced vital capacity and timed vital capacity data for each week were combined for each man in the same manner as the respiratory quotients. These values are reported at body temperature, environmental pressure and saturated with water (Table VI). At no time was the difference between the forced vital capacities of the two groups significant. When the timed vital capacities for one second of the control group were compared to the Spartase group there was no significant difference. There was a significant upward trend in a regression line fitted to the one second-timed vital capacity data for the Spartase group, but not in the case of the control group. The two second timed vital capacities indicated no significant changes in either group or between groups as the study progressed.

Maximum breathing capacity data for each week was combined for each man in the same manner as the respiratory quotients (Table VII). There was no significant difference between the two groups during any week during the study nor was there any significant trend as the study progressed.

Maximum breath holding time is also shown in Table VII. There were no significant differences between groups during any week. However, the Spartase group exhibited a significant upward trend in breath holding as the study progressed which the control group does not show.

Table VIII contains the mean hand grip data combined for each man each week. The control group exhibited an upward trend in the right hand grip as the study progressed but a test of significance fell just short of the 10% probability level. This was not seen in the left hand data for control or in either hand of the Spartase group. Only in week 9 was the control group right hand grip significantly higher ($P < 0.050$) than the Spartase group.

The "physical fitness indices" determined at the end of weeks 6, 7 and 9 are shown in Table IX. There was no significant difference between the two groups, for each period, even though there appeared to be some improvement.

Three points on the "neuromuscular excitability curves" were compared, at durations of 0.4, 1.0 and 10 milliseconds (Tables X - XII), for the measurements which were taken just prior to and immediately following the treadmill walk. The comparisons were made on the quantitative separation

of the muscle and nerve curves (milliamperes to stimulate muscle minus milliamperes to stimulate nerve). When the control group was compared to the Spartase group for each period, both before and after the walk, of the 48 comparisons made, only the "before exercise" measurements for week 2 (pre-therapy) at the duration of 10 milliseconds ($P < 0.10$) were significantly different (Table XII). The "before exercise" measurements were compared to the "after exercise" measurements for each week within each group. None of the 24 comparisons within the Spartase group showed a significance at the 5% level. Only 2 of the 24 comparisons within the control group showed significance at this level: week 2 at a duration of 10 milliseconds (Table XII), and week 4 at a duration of 1.0 milliseconds (Table XI).

Three points on the "neuromuscular excitability curves" were compared, also at durations of 0.4, 1.0 and 10 milliseconds (Table XIII), for the measurements which were taken just prior to and immediately following the exhausting treadmill run. When the control and Spartase groups are compared at each of the 3 durations, only the difference in the after exercise measurement at the duration of 10 milliseconds during the 6th week was significant. There was no significant difference during the last week of therapy.

Similarly, comparisons were made between before and after exercise measurements within each group. None of the 9 comparisons within the control group indicated a significant difference. However, 4 of the comparisons within the Spartase group were significant. During the 6th week, at 1.0 milliseconds duration, the difference in the measurements after the exercise were significantly higher than the difference between them before the exercise but here again the last week of therapy showed no significant difference. There was a significant difference during the last recovery period (no therapy) for all the 3 durations.

Using the procedure of Shaw, et al. (7) the data for the after exercise readings for weeks 2, 7 and 8 were converted to a coulomb and millisecond basis (Table XIV - XVI). Only the immediately after exercise data were used on the assumption that any beneficial effects of therapy were more likely to show up in the readings after exercise than before. Slopes and intercepts were calculated by the method of least squares for each man's muscle and nerve readings expressed in coulombs (y) and milliseconds (x). Only the motor slopes for week 2 (pre-therapy) showed a significant ($P < 0.050$) difference. For week 7 (the end of therapy) and week 8 (a post-therapy week) the difference did not achieve statistical significance at the 5% level.

Measurements done before and immediately after exhausting run were also compared at the levels of 0.4, 1.0 and 10 milliseconds. Of the 18 different comparisons between control and Spartase only one was significant ($P < 0.025$). This was for "after exercise" during the 4th week of therapy. No significant differences appeared during the next week, the 5th week of therapy.

Slopes and intercepts were also calculated for the "after exhausting run" data after converting to a coulomb and millisecond basis. In comparing the two groups only the muscle slopes for the 4th week of therapy were significantly different ($P < 0.025$).

Discussion

It has been observed in the present study that there were no significant differences between the control and Spartase groups (a) in oxygen consumption, carbon dioxide production, oxygen debt and RQ measurements during the brisk walk and the recovery periods, (b) in the pulse rates and physical fitness index during recovery after the exhausting run, (c) in maximal breathing capacity, and (d) in the timed vital capacity. As one would expect there was an improvement in the performance of men in both groups (i.e. lowered oxygen consumption) as the study progressed, which undoubtedly was directly related to training.

There was a significant upward trend in the one-second timed vital capacity for the Spartase group as the study progressed which was not observed in the control group. However, if the control week 2 was omitted, the upward trend for the remaining weeks was not significant. It should be pointed out that the first two weeks were training periods, both for the subjects and for the operator of the respirometer.

There was a significant increase in the Spartase group in breath holding during the last week of therapy and for the two weeks of recovery. This was due to two men who by chance, were both in the Spartase group. These men had a "private duel", beginning in the 6th week of the study and continuing throughout the remainder of the test. This introduced an additional factor of special personal motivation for these two individuals. One of the men increased his breath holding time tremendously, from 63 seconds to 119 seconds for the last week of therapy, and to 157 and 167 seconds, respectively, during the recovery periods or non-therapy periods. It should be pointed out that the maximum breath holding for the 4 other men in the Spartase group did not change appreciably.

There is little question that a run to exhaustion might impose sufficient stress to produce valid differences in the Rheotome measurements, but there is a question as to whether the fairly brisk walk would do so.

It seems reasonable to assume that the pre-therapy difference between the groups may have represented a real difference. But the differences became non-significant by the time the training effect was reflected in later weeks. This was true whether using the milliamp-millisecond curves or the coulomb-millisecond straight line. In short, the Rheotome measurements associated with the walking exercise do not provide any convincing evidence of beneficial effects from Spartase.

The results related to the run to exhaustion are similarly inconclusive. For both forms of expression of results there was a suggestion of difference between the groups in week 6 (a therapy week). However, in weeks 7 and 9 the differences were not significant at the 5% level.

The Rheotome utilized to measure performance must be carefully evaluated since there is a question as to the validity of "excitability" measurements. The Chesney and Tullis (10) report on Rheotome and neuromuscular fatigue raises many questions. It assumes that the size of the difference (MP-N) is a reflection of condition, yet the differences attributed to "normals" are smaller than those for "patients". The big question that arises is whether there is a physiological explanation for the larger differences after exercise than before exercise.

Shaw, et al. (7) claim to be treating physical fatigue in their study. They suggest that hyperexcitability of muscle and hypoexcitability of nerves (or the difference between the two) are related to athletic conditioning but one must realize that there is no proof that fatigue and excitability are related.

Excitability in both nerve receptors and neuromuscular junctions is probably a function of membrane permeability to potassium as affected by acetylcholine or similar substances. Athletic conditioning may well influence the receptors and muscle (motor) endplates by altering potassium or acetylcholine to alter excitability to each stimulus, but it is doubtful whether conditioning is related to susceptibility to fatigue or time of exhaustion. These are no doubt related to other factors in the body (i.e. level of oxygen debt) but not to nerve and muscular excitability. In other words, merely because nerve excitability is altered by athletic conditioning does not prove that excitability is related to physical fatigue. Shaw, et al. (7) have made no attempt to explain their results physiologically, which may be an impossible task, since there seems to be no physiological relationship between the aspartic acid salts and resting nerve-muscle excitability levels.

The performance of 12 men was evaluated during a 9 weeks "double blind" study where 6 men received placebos and the other 6 men received Spartase therapy. Under the conditions of this experiment there seemed to be no convincing evidence of the beneficial effects of Spartase therapy in humans,

in delaying the onset of exhaustion, as has been reported in previous studies in the literature. In reported studies, (1, 3, 4, 5, 6) it has been stated that the results of Spartase therapy are quite rapid, in that improvement in recovery from fatigue occurs within one week. The only significant changes in physiological measurements that occurred in this study were not observed until the 28th day of therapy, but were not present at the 35th day.

As expected there was a definite improvement in the performance of the men in both groups, as the study progressed, which can be directly related to the effects of training. During the study the men were questioned concerning their subjective responses and in all instances they did not seem to feel better. Very few of the men successfully guessed which therapy they were receiving.

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TABLE I

Weekly Body Weights of Subjects*

Body Weight, kg

Weeks	Control	Spartase
Pre Therapy		
2	79.16	75.62
Therapy		
3	79.18	75.82
4	78.69	75.71
5	78.63	75.57
6	78.88	75.28
7	78.85	75.74
Post Therapy		
8	78.75	75.72
9	78.75	75.41

* Mean of 6 men in each group. The average heights and ages of each group were the same, 175 cm for height and 28 years for age.

TABLE II

Mean Respiratory Quotient, During and After Exercise On Treadmill at 4.0 mph, 3.5% Grade

Week	15 Min Exercise*		1st 5 Min Recovery		2nd 5 Min Recovery	
	Control	Spartase	Control	Spartase	Control	Spartase
Pre-Therapy						
2	0.91	0.88	0.96	0.96	1.08	1.14
Therapy						
3	0.83	0.81	0.85	0.87	0.88	0.96
4	0.88	0.81	0.91	0.92	0.96	1.04
5	0.87	0.83	0.94	0.90	0.97	1.00
6	0.87	0.82	0.90	0.92	0.94	0.94
7	0.88	0.86	0.92	0.92	0.95	1.00
Post-Therapy						
8	0.90	0.88	0.94	0.98	0.97	1.06**
9	0.87	0.86	0.93	0.95	0.95	1.03**

* Measurements during the last half of total exercise period.
** Significantly higher than "Control" group ($P < 0.025$).

TABLE III

Mean Oxygen Consumption, During Exercise and Recovery*

Oxygen Liters/Minute

Week	15 Min Exercise		1st 5 Min Recovery		2nd 5 Min Recovery	
	Control	Spartase	Control	Spartase	Control	Spartase
Pre-Therapy						
2	1.57	1.63	0.59	0.59	0.27	0.24
Therapy						
3	1.60	1.67	0.55	0.60	0.27	0.27
4	1.60	1.67	0.58	0.59	0.25	0.27
5	1.71	1.66	0.61	0.59	0.31	0.27
6	1.69	1.66	0.58	0.59	0.31	0.27
7	1.61	1.60	0.55	0.56	0.30	0.26
Post-Therapy						
8	1.62	1.58	0.52	0.53	0.28	0.25
9	1.60	1.52	0.51	0.50	0.26	0.24

* Walking on treadmill at 4.0 mph, 3.5% grade.

TABLE IV

Carbon Dioxide Production During and After Walking Exercise

ml Carbon Dioxide/Minute

Weeks	Last 15 Min Exercise	5 Min Recovery	10 Min Recovery
		CONTROL	
Pre-Therapy			
2	1432	563	287
Therapy			
3	1331	467	237
4	1409	527	236
5	1491	574	302
6	1469	521	293
7	1420	509	283
Post-Therapy			
8	1459	491	269
9	1390	478	244
		SPARTASE	
Pre-Therapy			
2	1433	565	274
Therapy			
3	1336	519	258
4	1354	543	278
5	1379	526	270
6	1360	541	269
7	1377	518	258
Post-Therapy			
8	1389	518	267
9	1311	473	245

TABLE V

Oxygen Debt During Walk

Mean for Each Group in ml of Oxygen

Accumulated During Recovery

Weeks of Study	Control	Spartase
Pre-Therapy		
2	1886	1745
Therapy		
3	1719	1954
4	1781	1912
5	2271	1905
6	2127	2016
7	1913	1723
Post-Therapy		
8	1632	1457
9	1472	1290

TABLE VI

Mean Forced Vital Capacity and Timed Vital Capacity

	Forced Vital Capacity		Timed Vital Capacity			
	Liters		% in 1 Sec**		% in 2 Sec**	
Week	Control	Spartase	Control	Spartase*	Control	Spartase
Pre-Therapy						
2	5.41	5.19	70.2	74.0	90.7	94.7
Therapy						
3	5.46	5.25	82.0	83.3	92.6	95.1
4	5.45	5.18	81.2	82.9	92.2	95.5
5	5.51	5.21	79.8	84.5	91.6	95.3
6	5.44	5.17	81.1	84.5	92.4	96.0
7	5.42	5.20	81.3	84.5	92.6	95.1
Post-Therapy						
8	5.44	5.19	81.4	85.5	92.8	95.8
9	5.47	5.21	80.8	84.3	92.3	95.0

* Significant upward trend.
** Per cent of forced vital capacity.

TABLE VII

Mean Maximum Breathing Capacity

And Breath Holding Time

	Maximum Breathing Capacity Liters/Min		Breath Holding Time Seconds	
Week	Control	Spartase	Control	Spartase*
Pre-Therapy				
2	189	185	44	42
Therapy				
3	207	200	43	44
4	199	213	44	44
5	202	206	41	42
6	203	213	40	48
7	194	210	47	59
Post-Therapy				
8	208	213	46	67
9	218	224	48	66

* Significant upward trend.

TABLE VIII

Mean Hand Grip Pressure in Kg

	Right Hand		Left Hand	
Week	Control*	Spartase	Control	Spartase
Pre-Therapy				
2	55	51	48	47
Therapy				
3	57	52	48	48
4	56	52	47	48
5	57	50	47	48
6	58	52	47	49
7	59	51	48	48
Post-Therapy				
8	60	51	50	47
9	60**	50	50	48

* Significant upward trend.
** Significantly higher than Spartase.

TABLE IX

Physical Fitness Index*

Exhausting Run at 7.0 mph, 8.6% Grade

Weeks of Study	Group: Control	Group: Spartase
Therapy		
6	40.6	43.8
7	42.8	44.5
Post-Therapy		
9	42.7	46.0

* Using Harvard Scoring System -

$$\text{Index} = \frac{\text{Duration of Exercise in Seconds X 100}}{\text{2 X sum of pulses from 1 - 1}\frac{1}{2}\text{, 2 - 2}\frac{1}{2}\text{ and 3 - 3}\frac{1}{2}\text{ min after recovery}}$$

TABLE X

Rheotome Measurements Before and After Walking Exercise

Duration of Stimulus 0.4 Milliseconds

Mean Milliamperes Difference*

	Before Exercise		After Exercise	
Week	Control	Spartase	Control	Spartase
Pre-Therapy				
2	4.5	7.7	7.3	9.0
Therapy				
3	2.6	8.4	3.5	8.4
4	5.4	7.4	4.2	7.7
5	6.0	8.5	6.1	9.0
6	7.0	8.6	7.2	9.3
7	6.4	7.9	5.7	8.6
Post-Therapy				
8	6.5	9.4	7.6	8.7
9	7.0	10.0	6.6	8.2

* Difference to evoke stimulation of the motor point minus that of the nerve.

TABLE XI

Rheotome Measurements Before and After Walking Exercise

Duration of Stimulus 1.0 Milliseconds

Mean Milliamperes Difference

	Before Exercise		After Exercise	
Week	Control	Spartase	Control	Spartase
Pre-Therapy				
2	3.8	6.5	6.5	7.8
Therapy				
3	2.1	6.9	2.8	6.9
4	4.3	6.2	3.1*	6.9
5	5.0	6.5	5.3	7.1
6	5.5	6.9	6.2	7.3
7	5.5	6.4	5.0	6.7
Post-Therapy				
8	5.6	7.6	5.7	7.1
9	6.1	7.4	5.7	7.8

* Significantly lower than before exercise ($P < 0.010$).

TABLE XII

Rheotome Measurements Before and After Running Exercise

Duration of Stimulus 0.4, 1.0 and 10 Milliseconds

Mean Milliamperes Difference

Duration			Therapy		Post-Therapy
Msec	Time	Group	6	7	9
0.4	Before Exercise	Control	5.6	6.9	7.3
0.4	Before Exercise	Spartase	8.4	8.8	7.5
0.4	After Exercise	Control	6.0	7.1	8.4
0.4	After Exercise	Spartase	9.4	9.7	10.6**
1.0	Before Exercise	Control	5.0	5.9	6.4
1.0	Before Exercise	Spartase	6.4	7.0	6.5
1.0	After Exercise	Control	5.1	6.5	6.6
1.0	After Exercise	Spartase	9.1**	8.6	8.8**
10	Before Exercise	Control	3.8	4.0	4.1
10	Before Exercise	Spartase	5.0	5.3	4.9
10	After Exercise	Control	3.8	4.6	4.7
10	After Exercise	Spartase	6.7*	6.2	6.4**

* Significantly greater than "Control" group.
** Significantly greater than before exercise.

TABLE XIII

Rheotome Measurements Before and After Walking Exercise

Duration of Stimulus 10 Milliseconds

Mean Milliamperes Difference

	Before Exercise		After Exercise	
Week	Control	Spartase	Control	Spartase
Pre-Therapy				
2	2.1	5.0*	2.9**	4.8
Therapy				
3	1.5	5.0	2.3	5.3
4	3.0	4.2	3.3	4.8
5	3.1	4.3	3.7	5.0
6	3.6	4.7	4.1	4.3
7	3.8	4.8	3.7	5.1
Post-Therapy				
8	4.5	4.8	4.0	4.5
9	3.9	5.3	4.1	5.9

* Significantly greater than "Control" group.
** Significantly greater than before exercise ($P < 0.050$).

TABLE XIV

Rheotome Measurements Immediately After Walking Exercise*

	Motor		Nerve	
Week of Study	**Slope**	**y-Intercept**	**Slope**	**y-Intercept**
Week 2 (Pre-Therapy)				
Control	4.26	3.83	1.60	1.00
Spartase	7.00**	3.74	2.44	1.29
Week 7 (Therapy)				
Control	5.23	2.16	1.75	0.85
Spartase	6.99	2.89	2.13	0.95
Week 8 (Post-Therapy)				
Control	5.55	2.55	1.75	0.85
Spartase	7.58	2.87	2.56	1.11

* Slopes and y-intercepts calculated by least squares method for observations expressed in microcoulombs (y) and milliseconds (x).
** Control versus Spartase $P < 0.050$. All others non-significant.

TABLE XV

Rheotome Measurements Immediately After Running Exercise*

	Motor		Nerve	
Weeks of Study	Slope	y-Intercept	Slope	y-Intercept
Week 6 (Therapy)				
Control	5.63	2.21	1.98	1.00
Spartase	9.08**	2.91	2.58	1.07
Week 7 (Therapy)				
Control	6.67	2.66	2.19	1.13
Spartase	8.52	3.16	2.49	1.16
Week 9 (Post-Therapy)				
Control	6.61	2.65	2.07	0.87
Spartase	8.66	3.07	2.44	0.93

* Slopes and y-intercepts calculated by least square method for observation expressed in microcoulombs (y) and milliseconds (x).

** Control versus Spartase $P < 0.025$. All others were non-significant.

TABLE XVI

Rheotome Measurements

Difference Between Slopes After Run (Muscle-Nerve)

Groups	Weeks of Study		
	Week 6 (Therapy)	Week 7 (Therapy)	Week 9 (Post-Therapy)
Control	3.648	4.480	4.540
Spartase	6.503	6.035	6.220

* Slopes calculated by least squares method for observations expressed in microcoulombs (y) and milliseconds (x).

USA Medical Research & Nutrition Laboratory Proj #3A012501A803 Report #273

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This experiment was performed to evaluate the effects of administering Mg and K salts of aspartic acid (Spartase) as a possible means of increasing endurance in humans. Six men received placebos and six therapy over a six week period. A series of performance and condition measurements were applied during the experiment. No significant differences between the groups developed that could be attributed to the therapy.

1. Performance in Humans
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